Serial No.: 09/911,125
Docket No.: PHDE000244US (987.0006USU)

Remarks

Claims

Claims 1-15 are pending in the application.

Claims 9-11, 14, and 15 have been withdrawn from consideration pursuant to an election/restriction requirement.

Claims 1, 3-5, 7-8 and 13 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Kilmer (US 5,665,601).

Claims 1, 3-4, 6, and 13 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Gorog (US 5,916,813).

Claims 1-4 and 12 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Aghassi *et al.*, (US 2002/0182115 or US 6,489,171).

Claims 1-15 remain in the application unamended.

THE KILMER REFERENCE

Kilmer is directed to an aspirator/dispenser having a liquid interface detector, and an improvement therefor that avoids creating entrapped air bubbles in the liquid. See, Kilmer, c:1, l:6-8.

More specifically, at column 3, lines30 *et seq.*, Kilmer teaches adding an atmospheric vent line to line 20 through a valve that is normally open during the search for the fluid interface, but which closes after the air pressure line (22 in FIG. 1) is disconnected from the vessel.

In terms of a preferred construction, FIG. 2, a tip or vessel 103 is raised or lowered while it is connected to a line 120, which is connected to a pressure transducer detector 124 and a line 122 receiving a source of constant air pressure from a source such as compressed air 123, through valve 121 that is normally open as vessel 103 advances towards fluid such as serum 112 in container 140. (Any mechanism can be used to raise and lower vessel 103, for example a rack 130 and a driven pinion gear 132.) Once fluid 112 is contacted by vessel 103, a conventional piston pump 126 can be operated by, e.g., a stepper motor 141, to aspirate liquid into vessel 103, and then to dispense the aspirated liquid onto, e.g. a slide test element, or into another container (neither of which is shown).

What is added by the invention, is vent line 200 connected in parallel to vessel 103, by valve 202 connected to line 122, which is also connected to transducer 124.

Valve 202 is left open during liquid level sensing only. Vent line 200 exits to the atmosphere. Valves 202 and 121 are in turn connected to a conventional controller 210, which operates the valves in response to transducer 124, which can be, for example, a strain gauge silicon diaphragm relative pressure sensor.

In operation, the pressure P.sub.T of compressed air source 123 is delivered via valve 121 to both lines 120 and 200 (arrows 290 and 292) while vessel 103 is lowered, arrow 300, towards serum 112. Air expelled from tip orifice 260 of vessel 103, arrow 302, when it encounters serum 112, creates a spike of pressure in excess of P.sub.T, a spike that triggers transducer 124. This trigger sends a signal via controller 210 to shut off valve 121, removing the air pressure P.sub.T from entering further into line 120 and vessel 103. As a result, the air pressure in line 120 and vessel 103 above ambient, and specifically the triggering spike of pressure, is instantly released out through valve 202 and vent 200, arrow 292, instead of out vessel 103 into liquid 112. Shortly thereafter, for example 30 milliseconds, controller 210 shuts off valve 202 and activates motor 140, preferably after a pause, to cause pump 126 to aspirate some of serum 112 into vessel 103, without any air bubbles.

THE GOROG REFERENCE

Gorog is directed to an in vitro method of analysing the thrombotic and thrombolytic activity of blood. In particular Gorog relates to a method and apparatus for rapidly and simply assessing the capacity for shear-induced platelet aggregation in native blood. See, Gorog, c:1, l: 13-18.

At column 4, lines 9-47, Gorog teaches that the thrombotic activity analysing apparatus 2 comprises a capillary tube 4. In use, blood flows from the lower, and therefore inlet, end of the capillary tube 4 to the upper outlet end and thence to a collection reservoir 6. As illustrated in FIGS. 1 and 2 the collection reservoir 6 may conveniently be provided by inserting the capillary tube 4 into the barrel of a syringe 8 in which it is held by a silicon tubing collar 10.

Blood flow through the capillary tube 4 is caused by application of a negative pressure thereto. As illustrated the pressure may be conveniently provided by use of a Pasteur pipette 10 cut below the bulb and pushed into the upper end of the barrel of the syringe 8. The pipette 10 can be sealed to the barrel of the syringe 8 using UV curing glue. Prior to use the bulb 12 of the pipette 10 is compressed using a clip 14.

Gorog further teaches that the apparatus is prepared prior to blood-taking by compressing the bulb 12 of the pipette 10 with the foldback clip 14. The luer of the apparatus 2 is then inserted into the fitting of the catheter, the clip 14 removed and a stop clock started.

Removal of the clip 14 causes application of a vacuum in the syringe 10 which forces the blood to flow from the catheter through the capillary tube 4 into the syringe 10. In the capillary lumen, shear stress and platelet aggregation result in an occlusive thrombus formation which would eventually arrest blood flow.

The test is continued for a predetermined period of time, for example five minutes, after removal of the clip 14 and the syringe 10 (together as appropriate with the catheter) is then removed from the patient. The volume of blood in the reservoir 6 constituted by the syringe 10 is determined, preferably by means of a visual scale provided on the syringe 10. By comparison with a known range of blood volume for normal thrombotic reaction, an assessment can be made of the risk of bleeding or thrombosis which would be indicated respectively by larger or smaller volumes collected within the given time period.

THE AGHASSI REFERENCE

Aghassi relates to histological and molecular pathology and more specifically to an immunohistochemistry staining system for staining tissue samples with a variety of chemicals to facilitate examination of the samples. See, Aghassi, c:1,l:7-11.

Aghassi discloses a slide device 5 into which a tissue sample 6 may be placed. See, Aghassi, c:5, l:51-52. An open end 4 of a cassette 1 is preferably shaped to receive slide device 5. See, Aghassi, c:5, l:61-2.

When chemicals are injected into slide device 5, they preferably fill head space 10b and interact with tissue sample 6. Spacer 10a may be disposed about the entire perimeter of the slide device to surround the head space. See, Aghassi, c:6, l:7-9.

FIG. 3a depicts a top plan view of an interior portion of cassette 1. Slide device 5 is located in open end 4 of cassette 1 during the tissue staining process. A film 12 is preferably used to deliver chemicals to slide device 5 for application onto the tissue sample. See, Aghassi, c:6, l:33-37.

A plurality of containers 13a are preferably disposed on the film. Each container 13a preferably contains between about 50 microliters and about 200 microliters of chemical, and more preferably between about 100 microliters and about 150 microliters of chemical. See, Aghassi, c:6, l:52-57.

Guide rollers 15 preferably engage film 12 and rotate to move the film about the cassette and through the horseshoe-shaped loop depicted in FIG. 3a. The cassette preferably includes an injection system for injecting chemicals into injection port 17. The injection system preferably includes an injection piston 16 located near an end of slide device 5. Piston 16 is preferably attached to rotating shaft 18 via cam 59 which displaces the piston in a direction toward the film 12 at a location proximate the apex of the horseshoe-shaped loop. Piston 16 preferably reciprocates along an imaginary axis that extends longitudinally through injection port 17. Piston 16 preferably contacts container 19 and ruptures the container to release chemical into injection port 17. Injection port 17 and relief port 21 preferably communicate with the head space and may be disposed on opposite ends of the slide device. The piston preferably creates pressure is within injection port 17 to force the chemical through the injection port and into the head space 10b where it contacts the tissue sample. See, Aghassi, c:6, l:58 - c:7, l:9.

The time of contact between a chemical and a tissue sample may be predetermined by the spacing between containers on the film. Selected holders may be left empty to increase the spacing between adjacent containers, thereby lengthening the contact time between a given chemical and the tissue sample. In operation, the reciprocation of the piston and the movement of the film preferably occur at constant speeds and are synchronized such that the piston contacts each holder on the film. See, Aghassi, c:6, l:55-64.

A pressure-sensitive switch 31 is preferably located on top of cassette driver 25a. When cassette 1 is placed on top of cassette driver 25a, switch 31 is preferably depressed to activate motor 26. A timing device 32 is preferably used to stop motor 26 after a predetermined amount of time that is sufficient to allow a selected amount of chemicals to be applied to the tissue sample. See, Aghassi, c:7, l:56-63.

THE PRESENT APPLICATION

The present invention relates to transport of fluids, in particular for body-fluid analysis purposes.

In one embodiment, the fluid movement system 10 comprises a pressure generation unit 20 and a fluid movement area 30. The pressure generation unit 20 comprises a rubber bellow 40 supported by a spring 50. In this example, the spring 50 surrounds the rubber bellow 40, so that pushing or pulling the rubber bellow 40 has to be done against the restoring force of the spring 50. The rubber bellow 40 and the spring 50 are situated in a housing 60, whereby a movable press button 70 is situated in an opening on the upper side of the housing 60. The press button 70 attaches the rubber bellow 40 on its upper side, and might also be connected therewith.

The rubber bellow 40 is connected, preferably via a channel 80 that might also be part of the rubber bellow 40, to a valve chamber 90 as a further part of the pressure generation unit 20. The valve chamber 90 has a first valve 100 opened towards environment (i.e. outside of the fluid movement system 10), and a second valve 110 opened towards the fluid movement area 30. Both valves 100 and 110 are preferably flap valves. However, it is clear that any other valve type supporting the functioning of the fluid movement system 10, as described below, can be applied accordingly and might be selected dependent on criteria such as prize, ease of use, reliability or precision.

The rubber bellow 40 in conjunction with the mechanism of the spring 50 and the valves 100 and 110 constitutes a pressure chamber, which generally allows generating and maintaining a pressure, such as overpressure or underpressure, against the environment of the fluid movement system 10. Details will be shown and explained later.

The fluid movement area 30 comprises a sensor area 120 coupled (in the example of Fig. 1: abutting) to the valve chamber 90 via the second valve 110. The sensor area 120 is further coupled to a sample area 130 for receiving a fluid sample to be analyzed within the sensor area 120. Sensor elements 140 are located in the sensor area 120.

For operating the fluid movement system 10, a fluid sample is placed into (e.g. filled in) the sample area 130 and will be kept there, preferably under the influence of capillary forces or by additional valves. Because there is no initial pressure difference

inside of the fluid movement system 10 with respect to its environment, capillary force might be enough to prevent the sample fluid in the sample area 130 from dropping into the fluid movement area 30 before an underpressure is applied.
In the initial position of the fluid movement system 10, as shown in Figure 1, the rubber bellow 40 will be opened under the influence of the spring 50. The spring 50 also presses an inner flange 75 of the press button 70 against the inner top wall of the housing 60, thus acting as a stopper for the press button 70. The rubber bellow 40 thus has its maximum volume in this initial position.

For moving the sample fluid, located into the sample area 130, to the sensor area 120, the press button 70 will be pressed into the direction of arrow A, thus forcing the rubber below 40 to decrease its volume. The volume decrease of the rubber bellow 40 leads to an overpressure therein and thus into the valve chamber 90, which, again, closes the second valve 110 and opens the first valve 100, so that the overpressure can be released to the environment.

When the force into the direction of the arrow A will be removed, the spring 50, which has also been pressed down, will force the rubber bellow 40 to return into its initial position. This volume increase of the rubber bellow 40 driven by the spring 50 will lead to an underpressure in the rubber bellow 40 and thus into the valve chamber 90, which closes the first valve 100 and opens the second valve 110. This leads to an underpressure in the sensor area 120, which again will draw fluid of the fluid sample located in the sample area 130 into the sensor area 120 to the sensor elements 140.

The volume of the rubber bellow 40 should preferably be adjusted to the volume of the sample area 130, so that by releasing the underpressure, calibration fluid located over the sensor elements 140 can be completely removed and substituted by sample fluid. In case that e.g. a calibration fluid or gel has been situated on the sensor elements 140, it will also be removed from the sensor elements 140 under the influence of the underpressure.

While insofar the embodiment of Fig. 3A does not go beyond the principles as illustrated with respect to Figs. 1 and 2, the pressure generation units 20 of Fig. 3 further provides means for controlling the timing for moving the fluid(s). For that purpose, the press button 70 further comprises hooks 300 at its lower end. Corresponding locking means 310 are provided at the housing 60.

In the example of Figs. 3, each hook 300 comprises a ball 305 situated on a rod 307 having a smaller diameter than the outer diameter of the ball 305. Each locking means 310 comprises a spring-loaded leaf 315 with an opening 317 having a first shaping 318 allowing to receive the ball 305 and a second shaping 319 that cannot receive the ball 305. The leaf 315 is coupled to a spring clock mechanism 320.

Figs. 3B, 3D and 3E depict an initial position P0 of the locking means 310, wherein the leaf 315 is angled towards the hook 300. In that initial position P0, the ball 305 will 'see' the first shaping 318 of the opening 317, and can penetrate through when lowered in direction of angle A. However, once entered through the opening 317, the hook 300 (e.g. in combination with the flange 75 or other parts of the press button 70) will move the leaf 315 further towards a position P1. In this position P1 (cf. Figs. 3C-E), the rod 307 is located within the second shaping 319.

Once the pressure on the press button 70 in direction of arrow A will be removed, the spring 50 will force the press button 70 in its initial position. However, the spring clock mechanism 320, which has been activated when forcing from position P0 into position P1, will first keep the leaf 315 in the position P1 and slowly release to return to position P0. In a preferred embodiment, the spring clock mechanism 320 comprises a spring together with a gear mechanism, which when wound up will slowly return into its initial position, whereby the returning speed is dependent on the gear setting. Such mechanisms are well known in the art and need not be discussed here in detail.

As soon as the leaf 315 returns to position P0, the first shaping 318 of the opening 317 will release the ball 305 from the leaf 315, so that the press button 70 can also return into its initial position.

In other words, the shaping of the locking means 310 is provided in a way that when the hook 300 lowers towards the locking means 310, the hook 300 will first touch the locking means 310 in a first position that will not engage the hook 300. When the hook 300 is further moved into the direction of the arrow B, the locking means 310 will be forced under the influence of the hook 300 into a second position engaging the hook 300, so that it cannot return into its initial position once the force in direction of arrow A will be removed. The hook 300 will be locked e.g. by the converging opening 319 into the second position. Thus, the press button 70 will be kept down into a press down position and can first return to its initial position when

the locking means 310 will release the hook(s) 300. Controlling the release of the hooks 300 will therefore allow controlling the timing of the underpressure phase when the rubber bellow 40 will return into its initial position (thus generating an underpressure). By means of an external force, e.g. bending or moving the locking means 310, the hooks 300 can be released to initiate the underpressure. This external force can be controlled by the fluid movement system 10 itself or by a reading device.

THE CLAIMS DISTINGUISH PATENTABLY AND NON-OBVIOUSLY OVER THE PRIOR ART OF RECORD

Claim 1 is directed to a fluid movement system for moving a sample fluid comprising: pressure variation means for moving the sample fluid under the influence of a pressure variation applied to the fluid movement system, and timing means for controlling the timing for releasing a pressure in the pressure variation means.

Applicant respectfully asserts that none of the references teach all of the limitations of claim 1. As noted above, the present application provides that in one embodiment, timing means having a hook and leaf-spring combination as discussed in connection with Fig. 3, are provided to control the timing of the underpressure phase when the rubber bellow 40 will return into its initial position. Without the timing means, the rubber bellow 40 would freely expand under the influence of the spring 50 which ordinarily would simply force the rubber bellow 40 to return into its initial position after it has been pressed down.

As noted above, Kilmer teaches that once fluid 112 is contacted by vessel 103, a conventional piston pump 126 can be operated by, e.g., a stepper motor 141, to aspirate liquid into vessel 103, and then to dispense the aspirated liquid onto, e.g. a slide test element, or into another container. Such a conventional piston pump does not teach or suggest timing means for controlling the timing for releasing a pressure in the pressure variation means as set forth in claim 1. Specifically, the Office Action has not set forth how such a conventional piston pump teaches or suggests releasing any pressure.

Gorog teaches that prior to use the bulb 12 of the pipette 10 is compressed using a clip 14. Removal of the clip 14 causes application of a vacuum in the syringe 10 which forces the blood to flow from the catheter through the capillary tube 4 into

the syringe 10. Clearly, the timing of the blood flow is not controlled as the bulb expands freely once the clip has been removed.

Likewise with Aghassi, the Office Action has not identified timing means for controlling the timing for releasing a pressure in the pressure variation means. Aghassi teaches a pressure-sensitive switch 31 is preferably located on top of cassette driver 25a. When cassette 1 is placed on top of cassette driver 25a, switch 31 is preferably depressed to activate motor 26. A timing device 32 is preferably used to stop motor 26 after a predetermined amount of time that is sufficient to allow a selected amount of chemicals to be applied to the tissue sample. Such teachings relate to releasing chemicals from a selected number of containers 13a, which are applied to the tissue. Clearly, this does not teach or suggest controlling the timing for releasing a pressure as set forth in claim 1.

In light of the foregoing, Applicant respectfully submits that claim 1 is patentable over the prior art of record.

Claim 2 is directed to the fluid movement system of claim 1, further comprising a sensing element for sensing the sample fluid, wherein the pressure variation means is arranged for moving the sample fluid from and/or to the sensing element.

Applicant respectfully asserts that the Office Action has not identified any such sensing element in Aghassi. The Office Action appears to rely on tissue sample of Aghassi as the sensing element of claim 2. Clearly this is incorrect.

"Sensing" is defined in Random House Webster's Collegiate Dictionary as, *inter alia*, detecting mechanically, electronically, or photoelectrically. Aghassi does not teach or suggest, and the Office Action does not indicate any teachings thereing, how the tissue sample of Aghassi detects the chemicals applied to it. Rather the tissue sample merely received the chemicals.

In light of the foregoing, Applicant respectfully submits that claim 2 is patentable over the prior art of record.

Claims 3-5 depend from claim 1. For at least the reasons set forth above in connection with the patentability of claim 1, Applicant submits that claims 3-5 are patentable over the prior art of record.

Claim 6 is directed to the fluid movement system of claim 4, wherein the pressure variation means further comprises a resilient member for counter-acting against the volumetric variation applied to the volume-variation means.

As set forth above, the pressure generation unit 20 of the present invention comprises a rubber bellow 40 supported by a spring 50. In this example, the spring 50 surrounds the rubber bellow 40, so that pushing or pulling the rubber bellow 40 has to be done against the restoring force of the spring 50. By contrast, Gorog teaches that prior to use the bulb 12 of the pipette 10 is compressed using a clip 14. Such clip completely prevents the bulb from expanding. Only removal of the clip 14 causes application of a vacuum in the syringe 10 which forces the blood to flow from the catheter through the capillary tube 4 into the syringe 10. Accordingly, Applicant respectfully submits that Gorog does not teach or suggest a resilient member for counter-acting against the volumetric variation applied to the volume-variation means as set forth in claim 6.

In light of the foregoing, Applicant submits that claim 6 is patentable over the prior art of record.

Claim 7 is directed to the fluid movement system of claim 1, wherein the pressure variation means comprises: volume-variation means for successively generating an overpressure and/or an underpressure by means of a volumetric variation, a first valve for releasing the overpressure and/or for at least temporarily maintaining the underpressure, and a resilient member for counter-acting against the volumetric variation applied to the volume-variation means.

Applicant respectfully submits that the Office Action has not identified in the Kilmer reference, a resilient member as set forth in claim 7. Accordingly, Applicant submits that claim 7 is patentable over the prior art of record.

Claim 8 depends from claim 7. For at least the reasons set forth above in connection with the patentability of claim 7, Applicant submits that claim 8 is patentable over the prior art of record.

Claim 12 is directed to the fluid movement system of claim 1, wherein said fluid movement system is included in a cartridge to be inserted into a reading device.

Applicant respectfully submits that the Office Action has not identified in the Aghassi reference anything that would teach or suggest said fluid movement system being included in a cartridge to be inserted into a reading device as set forth in claim

12. Accordingly, Applicant submits that claim 12 is patentable over the prior art of record.

Claim 13 depends from claim 1. For at least the reasons set forth above in connection with the patentability of claim 1, Applicant submits that claim 13 is patentable over the prior art of record.

Conclusion

Applicant submit that claims 1-15 distinguish patentably and non-obviously over the prior art of record and are in condition for allowance. An early indication of allowability is earnestly solicited.

If any fees are due in connection with this application, authorization to charge deposit account 14-1270 for such fees is hereby provided.

Respectfully submitted,

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